At Mayo Clinic, researchers and clinicians are developing gene and cell therapies to treat brittle bone disease at its source. Among them is a physician in training who lives with the condition — and has endured more than 125 fractures. She came to Mayo to study under a pioneering physician-scientist who is breaking new ground in gene therapy. His decades of work are now moving closer to clinical trials.

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Video	Audio
	Dr. Ethel Aguirre Flores has spent her life proving what's possible and showing others they can do the same.
DR. AGUIRRE FLORES: [JHOW0170- 1:43-1:50] LOWER THIRD:	"I had my first fracture when I was 6 months old. And counting from then until now, over 125 fractures."
ETHEL AGUIRRE FLORES, M.D.	
MEDICAL GENETICS AND GENOMICS RESIDENT	
MAYO CLINIC	
[Photos from Dr. Aguirre Flores and broll of her in the lab]	She was born with osteogenesis imperfecta, also known as brittle bone disease. The rare genetic condition causes fragile bones that can break from even the slightest bump or fall.
DR AGUIRRE FLORES: [JHOW0170 - 1:50-1:57]	"Involving mostly my long bones — legs, arms — but also ribs and back."

	She's had 41 surgeries. Six metal rods hold her limbs together. Her most recent fracture happened just months ago while dancing.
DR. AGUIRRE FLORES: [JHOW0170 – 2:35-2:47]	"My most recent serious fracture was my left leg, the femur, just walking five years ago. It snapped without even falling."
	But what's <u>unbreakable</u> is her perseverance, determination and commitment to helping others.
	That drive brought her to Mayo Clinic, where she's completing her medical residency and studying under Dr. David Deyle. He's a clinical geneticist at the forefront of gene therapy. He has spent nearly 30 years advancing research in osteogenesis imperfecta.
DR. DEYLE [JHOW0172 - 0:58-1:07] LOWER THIRD: DAVID DEYLE, M.D. CLINICAL GENOMICS MAYO CLINIC	"My lab is primarily geared on treating individuals with genetic disorders, both with cell therapy and gene therapy."
DR. DEYLE [JHOW0172 – 3:00-3:09]	"We also have gene editing, where you use another protein to actually alter a gene sequence, to either correct it or to knock it out."
	And that's the same kind of breakthrough Dr. Deyle and his team are pursuing. Inside his lab, researchers are working to do what medicine has never done — treat brittle bone disease at its genetic source. The challenge is getting the therapy into the bone to fix the mutation.

DR. DEYLE: [JHOW0172 –8:10-8:26]	"We have to be able to get that process into the bones and correct the bones at the source. Because there's no way to do a transplant or anything for your bones, you have to go and try to fix them at its source essentially."
	The root of the problem is a genetic mutation that causes the body to produce faulty collagen. Collagen is the protein that gives bones their strength.
DR. DEYLE [JHOW0172 – 7:29-	"Osteogenesis imperfecta is caused by a mutation in one of the genes that makes a building block of bones. And what happens is that building block is bad, and so we have to get rid of it. We use a protein that will then knock it out or get rid of that copy. So what's left is normal, and the bone should be improved as far as your overall structure and strength."
	He's developing two treatment approaches: a small molecule therapy to improve bone density and a gene editing strategy to eliminate the faulty gene altogether. His work is inching closer to clinical trials.
DR. DEYLE [JHOW0172 – 4:19-4:27]	"I really want to be able to provide a treatment that's going to help them, long term, reduce the risk of fractures and help them grow better."
	His team is applying the same precision to other rare genetic disorders — using tailored strategies to correct genetic mutations and rebuild tissue.
	And some of the most determined minds behind this research in Dr. Deyle's lab know these conditions firsthand — including Dr. Ethel Aguirre Flores. She's the third person with brittle bone disease to train in Dr. Deyle's lab.
DR. DEYLE: [JHOW0173 – 2:36-2:49]	"She's very smart, knowledgeable in her field, and you can kind of tell, based on her history, that she's kind of a

	fighter, right, and that she is going to put everything, all of her effort, into it because of her history."
	Dr. Aguirre Flores was born and raised in Mexico, the only girl of four siblings. Her family encouraged her to chase every dream.
DR. AGUIRRE FLORES [JHOW0170 – 4:07-4:11]	"They would always let me know anything's possible. You can do anything you want."
	She knew at age 8 she wanted to be a pediatric doctor — to care for children with conditions like hers.
DR. AGUIRRE FLORES: [JHOW0170 – 8:47-8:57]	"Treating children with congenital disorders as a whole, and helping them grow, live their childhood to the best."
	In June, she'll graduate from Mayo Clinic's medical genetics and genomics residency — and begin her next chapter as a pediatric geneticist —a reminder that even the toughest paths can lead exactly where you're meant to be.
DR. AGUIRRE FLORES [JHOW0170 - 8:12-8:20]	"I hope that my story brings hope and inspires others to not put limits on themselves try always to achieve their dreams, keep fighting for their dreams."
	For the Mayo Clinic News Network, I'm Susan Murphy.